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OFFICE OF NAVAL RESEARCH

FINAL REPORT

May 13, 1992

PUBLICATIONS/PATENTS/PRESENTATIONS/HONORS/STUDENTS REPORT

for

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Design and Synthesis of Molecular Systems Capable of Supporting Intracavity Chemical Reactions.

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10 May 1992

Part I

a. Papers Submitted to referreed Journals:

1,. J. E. Cochran, B. W. Whitlock and H. W. Whitlock, "The Pi-Hydrogen Bond Stabilizes Intracavity Complexes.", Submitted to J. Amer. Chem Soc.

b. Papers Published.

1. B. J. Whitlock & H. W. Whitlock, "Catalytic Activity via Hydrophobic Host-Guest Complexation", Tetrahedron Letters, 6047 (1988)

2. B. P. Friedrichsen & H. W. Whitlock, "Concave Functionality: Intracavity Phosphine Oxides", J. Amer Chem. Soc., *111* 9134-9134 (1989)

3. B. J. Whitlock & H. W. Whitlock, "Concave Functionality: Design Criteria for Nonaqueous Binding Sites", J. Amer Chem. Soc, 112, 3910-3915 (1990)

4. K. Neder & H. W. Whitlock, "Effect of Basicity on Pyridine-Based Hosts as Intracavity Hydrogen Bond Acceptors", Submitted to J. Amer. Chem. Soc. J. Amer Chem Soc., 112, 9412-9414, 1990

5. B.P. Friedrichsen & H.W. Whitlock, "Endo-Phosphine Oxide Functionalities as Reaction Locus in Concave Hosts"., B. P. Friedrichsen D. R. Powell, H. W. Whitlock, J. Amer Chem. Soc., 112, 8931-8941, 1990

6.J. E. Cochran, T. J. Parrott, B. J. Whitlock, H. W. Whitlock, "π Hydrogen Bonds as a Design Principal in Molecular Recognition", *J. Amer. Chem. Soc.*, **1992**, *114(6)*, 2669-2670.

c. Books Published: None

d. Books Submitted for Publication: None

e. Technical Reports & Non-Referreed Papers: None. (Technical Summaries for the above publications will be submitted in the near future.)

f. Patents Filed: None.

g. Patents Granted: None.

h. Invited Presentations

1. Symposium on Host-Guest Chemistry, University of Illinois, April 1989.

2. Mini-Symposium on Molecular Recognition, University of Michigan, October, 1989.

3. Symposium on Host Guest Complexes, American Chemical Society National Meeting, Atlant Ga., April 10-15, 1991. A review of our NAvy-Supported work on Intracavity Functionalization.
i. Contributed Symposia: None.

j. Honors/Awards. None.

k. Number of Graduate Students with ONR Support. Total is 2; Minority is 1; Asian is 1.

l. Postdoctoral Fellows. Total is 1; Minority is 0; Asian is 0.

m. Other Funding
1. N.S.F Hydrophobic binding in Hosts, $100,000, Oct 1989-Oct 1990

Part II

Principal Investigator: Howard W. Whitlock, Jr.
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Brief Project Description

This project involves the synthesis of molecules containing concave functional groups capable of supporting chemical reactions. Salient sub-problems have to do with the distinction between steric encumbrance and steric hindrance, and with development of well documented intracavity covalent bond-forming reactions. Host molecules bearing functional groups capable of hydrogen bond formation, metal ion complexation, and aldimine condensation are of primary interest, their functional groups being in a sterically encumbered but not hindered environment. The structural motif involves construction of cyclophanes bearing the desired reactive group oriented in an inward-pointing manner, in combination (optionally) with structural features that enhance binding of the external co-reactor.

Recent Significant Results

1. (Submitted) While hydrogen bond formation is generally considered to be the principal way of stabilizing intracavity complexes, we have shown that edge-face π-Hydrogen bonds, arising from edge-face aromatic-aromatic stacking, can be an effective stabilizing force. Several XRay structure and variable temperature studies have confirmed the importance of this in high-effeciency hosts.

2. (Published) Complexation of metals with endo-phosphine oxides shows a smooth continuity in steric repulsion of guest as size of external co-reactant is increased. Stable endo-bound metal complexes have not been prepared. Endo-Schiff bases have so far eluded us but synthesis is still active.

3. (Published) Remarkably high association constants result from incorporation of benzo bridges into the basic underlying cyclophane. This is particularly important as the aromatic rings may serve as carriers for functional groups involved in catalytic activity. This is an important point; the accurate placing of reactive/catalytic groups is an important (and difficult) problem in this area.

Coworkers: B.J. Whitlock
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